

REMARKS

The Office Action and the cited and applied references have been carefully reviewed. No claim is allowed. Claims 1, 3, 5-12, 17-19, and 22-25 presently appear in this application and define patentable subject matter warranting their allowance. Reconsideration and allowance are hereby respectfully solicited.

Claim 19 has been rejected under 35 U.S.C. §112, second paragraph, as being indefinite. Claim 19 is now amended to recite that it is the spacer that is selected from the group consisting of an amide bond, an ether bond and a sulfide bond, thereby obviating this rejection.

Claims 1, 5, 8, 11, 19, 23, and 24 have been rejected under 35 U.S.C. §102(b) as being anticipated by Dickerson et al., U.S. Patent No. 5,677,276. This rejection is respectfully traversed.

Claim 1 is amended to recite that the therapeutic agent for joint diseases covalently binds to the carboxyl group of hyaluronic acid or a derivative or salt thereof, as supported in the specification at page 24, line 23 to page 25, line 21. By contrast, in the conjugate of Dickerson, it is the hydroxyl group that is used as the binding site (see Figs. 1 to 3 and the Examples), not the carboxyl group. There is simply no disclosure, teaching or suggestion on how to synthesize conjugates of the present invention in which the therapeutic

agent binds to hyaluronic acid at the carboxyl group via a spacer. Accordingly, Dickerson cannot anticipate the presently claimed invention.

Furthermore, as acknowledged by the examiner in the §103(a) rejection on page 3 of the Office Action, Dickerson does not teach or suggest the administration of Dickerson's compounds to treat joint diseases.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 1, 3, 5-12, and 17-25 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Dickerson et al., U.S. Patent 5,677,276, and Gallardy et al. (WO 92/09556).

Dickerson does not disclose, teach or suggest that a therapeutic agent for joint diseases binds to a carboxyl group of hyaluronic acid via a spacer. Indeed, compared to the presently claimed conjugate, the conjugate of Dickerson has a different therapeutic agent (RGD peptide) bound to hyaluronic acid at a different site on hyaluronic acid (Dickerson does not even suggest the applicability of other binding sites).

Gallardy is applied by the examiner simply for compounds that have utility in promoting wound healing. However, Gallardy does not satisfy the deficiency in Dickerson noted above and the combination of Dickerson and Gallardy could not have led those of ordinary skill in the art to arrive at the presently

claimed conjugate in which a therapeutic agent for joint disease binds to hyaluronic acid at a carboxyl group via a spacer.

Moreover, the presently claimed conjugate has demonstrated synergistically improved efficacy of hyaluronic acid and the therapeutic agent for joint diseases, as disclosed in the specification in the paragraph bridging pages 7 and 8 and in Experiment 6 on page 62, lines 9-22. Such surprisingly superior results cannot be made obvious by Dickerson's and Gallardy's combined disclosures and teachings.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 1, 3, 5-12 and 17-25 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Dickerson, and Gallardy in further view of Bemis et al. (U.S. Patent 6,147,080) or Wunderlich et al. (U.S. Patent 6,066,332). This rejection is respectfully traversed.

The secondary references, Bemis and Wunderlich, are only applied for their teachings of COX-2 inhibitors and ibuprofen which can be used to treat joint diseases such as rheumatoid arthritis and osteoarthritis. However, the teachings of Bemis and Wunderlich cannot satisfy the deficiencies of the Dickerson reference as discussed above. Therefore, the present invention is patentable for the same reasons as in the obviousness rejection discussed immediately above.

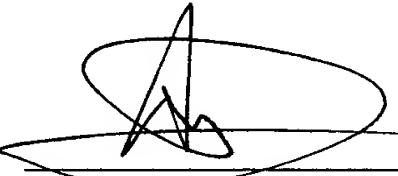
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Reconsideration and withdrawal of the rejection are therefore respectfully requested.

In view of the above, the claims comply with 35 U.S.C. §112 and define patentable subject matter warranting their allowance. Favorable consideration and early allowance are earnestly urged.

Respectfully submitted,

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